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EXAMINER	
MOORE, SUSANNA	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,951	NAKAZATO ET AL.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *9-15 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/4/08,7/5/06,11/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 7/7/2008 is acknowledged. Group I, drawn to thieno[3,2-b]pyrimdines, and simple compositions thereof, embraced by claims 1-8, 16(part) and 17 was elected by Applicant. The traversal is on the ground(s) that the restriction is nimproper by stating, "The instantly claimed compound is "an antagonist against CRF receptor which is effective as a therapeutic or prophylactic agent for disease in which CRF is considered to be involved." Lines 14-15, page 2 of Specification. In contrast, the compound taught by U.S. Patent No. 6,339,089 is "useful for pharmacotherapeutically ameliorating arterial blood oxygen partial pressure." Lines 12-13, column 1. Clearly, the technical background of the instant invention is entirely different from that of U.S. Patent No. 6,339,089. One of ordinary skill in the art who was looking for an improved antagonist against CRF receptor would not have been motivated to consult any prior art references concerning compounds that are taught as useful for pharmacotherapeutically ameliorating arterial blood oxygen partial pressure. Therefore, the cited reference is not proper for the assessment of the special technical feature of the instant invention." This is not found persuasive because the special technical feature as defined by the compound core presented by Applicant is present in the '089 patent, regardless of the intended use. The lack of unity requirement is deemed proper and is therefore made **FINAL**.

There are 18 claims pending and 10 under consideration. Claims 1-8 and 16 are compound claims. Claim 17 is a composition claim. Claims 9-15 and 18 are nonelected subject

matter. This is the first action on the merits. The application concerns some thieno[3,2-b]pyrimidine compounds and simple compositions thereof.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the international application on 1/6/2005. It is noted, however, that the certified copy was misplaced. There is only a certified copy of the abstract in the file.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted Thieno[3,2-b]pyrimidines as CRF Receptor Antagonists. This is just a suggestion. Please feel free to change the title to accurately define the invention.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 1/4/2008, 11/27/2008 and 7/5/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objections

Claim 1 is objected to because of the following informalities: the fourth line from the last line in claim 1 recites, "r is 1 or 2)." The "2)" should be replaced with "2." Appropriate correction is required.

Claim 17 is objected to because of the following informalities: Claim 17 is substantial duplicates of claims 1-8 and 16, as the only difference is a statement of intended use, which is not given material weight. Note *In re Tuominen*, 213 USPQ 89. Appropriate correction is required.

Note: Applicant is reminded of the manner of making amendments.

37 CFR § 1.121 Manner of making amendments in application.

> (c) Claims. Amendment to a claim must be made by rewriting the entire claim with all changes (e.g., additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an exiting claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims in the amendment document will serve to replace all prior versions of the claims in the application, In the claim listing, the **status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)**.

The following claim(s) fail to properly identify the status of the claims: claims 1-18 have been amended in the response filed 7/5/2006, but the claims submitted on 7/19/2007 do indicate a preliminary amendment. Amended claims will not print properly if the status identifier is not properly stated, i.e. (Currently amended).

This application contains claims 9-15, 16(part) and 18, drawn to an invention nonelected with traverse in the paper of 7/7/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The word "derivative" is vague. A derivative is a substance or compound obtained from, or regarded as derived from, another substance or compound. What are these derivatives? Are the"derivatives covered by the scope of the genus of formula (I)?

Regarding claim 17, the preamble is drawn to a compound but the claim language embraces compositions, i.e. "active ingredient." What does Applicant intend? If Applicant intends a composition, then an excipient, carrier and/or diluent should be added to the claim. If Applicant intends a compound, claim 17 does not further limit claims 1-16.

Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for racemic isomers, does not reasonably provide enablement for "isomers." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in

scope with these claims. There are many different kinds of isomers, e.g. regioisomers, constitutional isomers, stereoisomers, etc. Constitutional isomers are isomers with different connectivity that have the same molecular formula. For example, n- propanol and methyl ethyl ether have the same molecular formula, C_3H_80 and differ greatly in structure-connectivity and properties. Thus, said claims are not enabled for the term "individual isomers," and as such, the phrase should be removed from said claims.

Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound of claim 1 or pharmaceutically acceptable salts of said compounds does not reasonably provide enablement for a hydrate of a compound of claim 1. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention is a compound of claim 1, or a pharmaceutically acceptable salt of said compound. There is no teaching of hydratesor solvates of the compounds of claim 1 in the specification.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "hydrate" found in the claims is defined as a compound formed by solvation (the combination of water molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound (See Vippagunta, et al.)

The scope of "hydrate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active in vivo. Solvates and hydrates cannot

always be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular hydrate or solvate.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention.

The breadth of the claims

The breadth of the claims is a conjugate of claim 1 or a pharmaceutically acceptable salt or solvate thereof.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make solvates of a conjugate of claim 1 it would require undue experimentation to figure out the solvents, temperatures and reaction times that would provide solvates of the above compounds.

To overcome this objection, Applicant should submit an amendment deleting the term "hydrates."

Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is the Wands factors, which are used to evaluate the enablement question. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace thieno[3,2-b]pyrimidine compounds. The scope of "prodrug" is not adequately enabled. Applicants provide no guidance as how the compounds are made more active in vivo. The choice of a "prodrug" will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrugs will be suitable for the instant invention.

The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would no how to prepare the various compounds suggested by claim 1. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. Applicant is enabled for esters and amides as prodrugs since said substituents, as defined by X, are embraced by claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakazato et. al. (US 6852732 B2).

The instant invention claims compounds of formula (I), wherein Ar= 2,4-dichlorophenyl; Y= nitrogen; n= 0; m=0; X= hydroxy, cyano, CO_2R^8 or $CONR^9R^{10}$; R^6= methyl; R^8, R^9, R^{10}, R^7, R^4 and R^5= hydrogen; and the nitrogen ring is a 6-membered unsaturated nitrogen ring, piperidine, and simple compositions thereof.

The reference teaches compounds of formula (I), wherein Ar= 2,4,6-trimethylphenyl; Y= nitrogen; n= 0; m=0; X= 2-ethyl; R^6, R^8, R^9 and R^{10}= methyl; R^7, R^4 and R^5= hydrogen; and the nitrogen ring is a 6-membered nitrogen ring, piperidyl-3-ene, and simple compositions thereof. See columns 47-48, compounds 11-01-11-03 and column 66, claim 3.

The difference between the reference and the instant Application is the piperidine ring, unsaturated versus Applicant's saturated. The reference teaches the nitrogen ring can be saturated or unsaturated, see column 2, subformula (III). Thus, the unsaturated and saturated ring systems are alternatively useable. Thus, said claims are rendered obvious by Nakazato et. al.

This rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. This rejection might also be overcome by showing that the copending application is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624